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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,209	01/16/2001	James E. Hildreth	JHU1290-7	5480

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EXAMINER	
NAVARRO, ALBERT MARK	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/761,209	Hildreth
Examiner	**Art Unit**
Mark Navarro	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____ .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 8-17 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 8-17 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 1 1/2
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Applicant's preliminary amendment filed January 16, 2001 (Paper Number 1 ½) has been received and entered. Claims 1-7 and 18-23 have been canceled, consequently claims 8-17 are pending in the instant application.

Claim Rejections - 35 USC § 112

1. Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claim is directed to methods of ameliorating an immune response mediated disorder in an animal wherein the disorder is AIDS, autoimmune disease, and graft rejection.

Applicant's specification contains insufficient guidance to one of skill in the art for the treatment of AIDS, autoimmune disease and graft rejection. The specification provides no description of critical parameters for administering antibodies in order to achieve a desired therapeutic outcome. General protocols for effective antibody-based treatment of AIDS, autoimmune disease, and graft rejection have not yet been established in the art. The specification does not describe what, if any, clinical changes or benefits are manifested as the result of monoclonal antibody-mediated individuals suffering from AIDS, autoimmune diseases or graft rejection such that one of skill in the art could determine the efficacy of the claimed invention. Undue experimentation would be required of one of skill in the art to practice the

claimed methods relying only on the teachings of the instant specification for guidance in view of the current state of the art to which the invention pertains.

The obstacles to the development of therapeutic approaches with regard to the treatment of HIV-1 infection in humans are well documented in the scientific literature. Theses obstacles include the fact that the modes of viral transmission include virus-infected mononuclear cells which pass the infecting virus to other cells in a covert form, as well as via free virus transmission, the existence of a latent form of the virus, the ability of the HIV-1 virus to hide in the central nervous system where blood cells and neutralizing agents carried by the blood cannot reach the retrovirus due to the blood-brain barrier, and the complexity and variation of the elaboration of the disease. The status of immunobased therapies in HIV infection and AIDS is summarized in a review article by Fahey *et al* (Clin. Exp. Immunol. Vol 88, pp 1-5, 1992), cited of interest, Fahey *et al* teach that clinical benefit in trials using different approaches to immune-based therapies have not achieved a great deal of success. Table 1 on page 2 summarizes the results obtained in trials using numerous different types of immune-based therapies and teaches that antibody-based therapies involving the administration of immune serum gamma globulin or murine anti-gp160 monoclonal antibodies did not achieve clinical change or benefit. In view of the lack of working examples, and the lack of success which has been achieved to date in the use of immune-based therapies in general, and of antibody-based therapies in particular, for therapy of HIV-1 infection, one of skill in the art would be forced into undue experimentation to practice the broadly claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

2. Claims 8-9, 11, and 13-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Arfors.

The claims are directed to a method of ameliorating an immune response mediated disorder in an animal which comprises: administering to the animal a therapeutically effective amount of an antibody, capable of suppressing intercellular leukocyte adhesion, wherein the antibody binds to an epitope on the leukocyte adhesion receptor β-chain.

Arfors (U.S. Patent Number 4,797,277) disclose of a method for treating mammalian organs suffering from ischemia in order to prevent ischemia/reperfusion-induced tissue damage, which involves administering anti LAR-β chain-specific monoclonal antibody 60.3. (See column 2). The examples describe parenteral administration at a dose within the range specified in claim 15.

No distinctions are seen between the claims and the reference.

3. Claim 8 is rejected under 35 U.S.C. 102(b) as being anticipated by Vedder *et al.*

Vedder *et al* (J. Clin. Invest. Vol. 81, pp 939-944, 1988) disclose of a method for reducing leukocyte-mediated organ injury by administering anti-CD18 monoclonal antibody 60.3.

No distinctions are seen between the claims and the reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 8-9, 11 and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arfors or Vedder *et al* in view of Springer *et al.*

Arfors and Vedder *et al* each teach that anti-CD18 monoclonal antibodies such as 60.3 inhibit leukocyte adherence functions and inhibit ischemia-reperfusion injury and speculate that these findings may be relevant to the therapy of many clinical disorders that result from ischemia and reperfusion including organ transplantation.

Neither Arfors or Vedder *et al* teach of LFA-1 or proteins capable of competing for receptors and of inhibiting cell to cell binding.

Springer *et al* (WO 88/06592) teach that the administration of LFA-1 or proteins capable of competing for receptors and of inhibiting cell to cell binding were recognized to have potential applicability for treatment of autoimmune diseases and graft rejection. (See page 12).

It would have been *prima facie* obvious to combine the teachings of the cited prior art and to administer anti-CD18 monoclonal antibodies such as Mab 60.3 which had been shown to inhibit cell adhesion, for the purpose of treating autoimmune diseases and graft rejection. One of ordinary skill in the art would have been motivated to do so in view of the teaching of Springer *et al* and Vedder *et al* as previously characterized.

5. Claims 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arfors, Vedder *et al* and Springer *et al* as applied to claims 8-9, 11 and 13-15 above, and further in view of Hildreth *et al.*

Arfors, Vedder *et al* and Springer *et al* do not teach of the monoclonal antibody produced by ATCC HB X.

Hildreth *et al* (J. Immunology Vol. 134 pp 3272-3280, 1985) teach of the monoclonal antibody H52, which is the same antibody produced by the hybridoma cell line ATCC HB X. (Specification page 5).

It would have been *prima facie* obvious to substitute H52 into the methods suggested by the combined teachings of Arfors, Vedders *et al* and Springer *et al.* One of ordinary skill would have been motivated to do so in view of the teaching of Hildreth *et al* that Mab H52 had been shown to inhibit all T cell functions tested in a manner similar to the prior art Mab 60.3 which had been shown to be effective for inhibiting ischemia/reperfusion injury.

6. Claims 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arfors, Vedder *et al* and Springer *et al* as applied to claims 8-9, 11 and 13-15 above, and further in view of Pastan *et al.*

Arfors, Vedder *et al* and Springer *et al* do not teach of monoclonal antibodies labeled with a radioisotope, drug, lectin, or a toxin.

Pastan *et al* (Cell Vol. 47, pp 641-648, 1986) teach that the concept of using immunotoxins for the treatment of autoimmune disease, in autologous bone marrow transplantation and to improve organ graft survival. (See pages 645-6).

It would have been *prima facie* obvious to combine the teachings of the cited prior art and to produce conjugates comprising anti-LAR-β chain specific monoclonal antibodies and cytotoxic moieties and to use such conjugates in methods for treating autoimmune diseases and organ transplantation. One of ordinary skill in the art would have been motivated to do so in view of the combined teachings of Pastan *et al*, Arfors *et al*, Vedder *et al*, and Springer *et al* as previously discussed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 8-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,888,508. Although the conflicting claims are not identical, they are not patentably distinct from each other because each set of claims encompasses methods of ameliorating an immune response comprising administering a monoclonal antibody produced by ATCC HB X/10160.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro, whose telephone number is (703) 306-3225. The examiner can be reached on Monday - Thursday from 8:00 AM - 6:00 PM. The examiner can be reached on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Lynette Smith can be reached at (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1645 by facsimile transmission. Papers should by faxed to Group 1645 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703) 308-4242.

Mark Navarro

Primary Examiner

December 13, 2001